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National Institutes of Health (U.S.)
Division of Research Services

Annual report and program activities

Division of Research Services FY 1985 Annual Report

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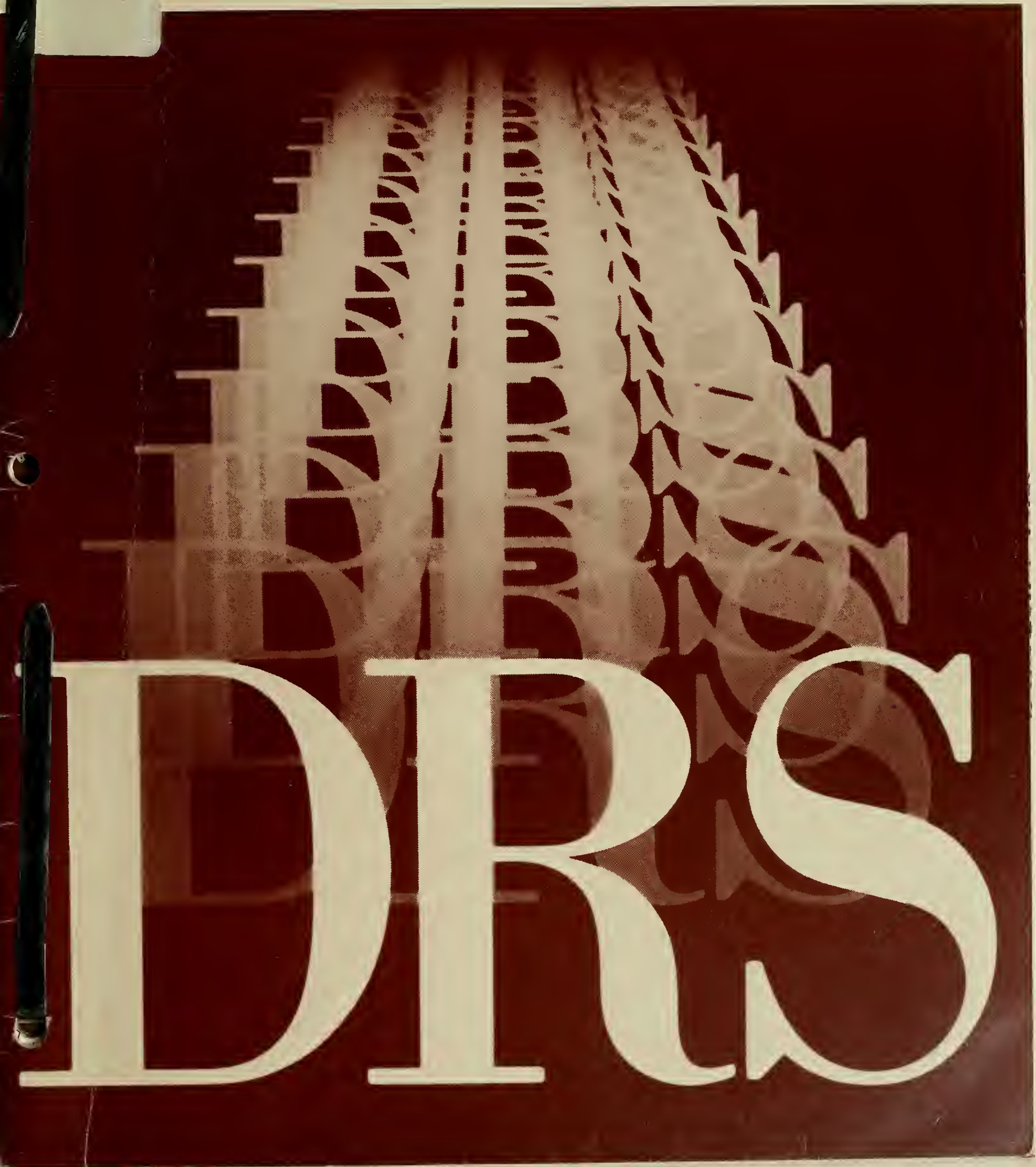
National Institutes of Health



The Division of Research Services

The many specialized functions of the Division are designed to support all of the 18 Bureaus, Institutes, and Divisions (BIDs) which constitute the National Institutes of Health. The primary program emphasis, however, is directed at serving the 8,000 staff members of the intramural program, including more than 2,600 doctoral level scientists who conduct research in NIH laboratories.

Organizationally, the Division is structured to provide products and services in support of the sequential steps in every biomedical research project: planning, making available models and substrates, manipulating and measuring research materials, and recording and communicating research results.

- The Library Branch possesses or has access to virtually all published biomedical knowledge to assist the investigator in planning and designing his/her project.
- The Veterinary Resources Branch provides the animal models, organic materials, and proper facilities for their use.
- The Biomedical Engineering and Instrumentation Branch collaborates with the investigator in devising the means whereby research materials may be manipulated and results measured, often with highly sophisticated electronic equipment.
- Finally, the skills of the Medical Arts and Photography Branch are available to all investigators to enable them to record the results of their research and communicate them to the scientific community.

Division of Research Services

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A Letter From the Director

Robert A. Whitney, Jr., D.V.M.,
Director
Division of Research Services
National Institutes of Health

In his final contribution to a DRS Annual Report last year, our former Director, Dr. Joe Held, thanked the DRS managers and employees for their enduring cooperation. Their teamwork, he pointed out, enables the Division to provide high quality services and products to the NIH intramural programs as effectively and economically as possible.

While serving as Acting Director and, more recently, as Director of DRS, I have found my tasks lightened by that spirit of teamwork as we press forward with a number of initiatives to maintain DRS's effective and economical delivery of high quality services. These activities include projects initiated by DRS and also our implementation of NIH-wide initiatives.

In keeping with the efforts of the Department of Health and Human Services to reduce its number of full-time equivalent positions (FTEs), DRS had adopted the goal of a 12-percent reduction in FTEs by the end of FY 1987; the plan included a 5 percent reduction by the end of FY 1985. The 1985 goal has been met. To reduce FTEs by 12 percent without sacrificing the quality of our services to intramural investigators is a real challenge, and the DRS branches and Office of the Director are improving efficiency and productivity to accomplish it.

The management of Scientific Equipment Services (SES) in the Biomedical Engineering and Instrumentation Branch (BEIB) established an employee productivity committee—with no supervisory participants—to identify problems and suggest solutions that could improve SES services to NIH investigators in fabricating, repairing, and renting equipment. The committee has made a number of recommendations that are being put into effect. For example, the committee pointed out that SES office personnel could respond much more efficiently to investigators' inquiries about the status of work being done for them if job status information were available from an on-line computer system. SES is establishing an automated system that meets this need and also makes it easier for shop managers to expedite jobs, reducing turnaround time.

For many years the NIH Library has benefited from the suggestions and other help of its Advisory Committee, representing the NIH intramural scientific community. Other DRS branches have now inaugurated similar committees to keep them fully informed of their users' needs and priorities.

Currently all four branches, in conjunction with the Office of the Director, are either planning or actually conducting productivity studies, performed primarily by contractors hired with evaluation set-aside funds. In addition, the Small Animal Section and the Carnivore Unit of the Veterinary Resources Branch have conducted special studies of their users' plans and future needs, so as to tailor their programs to those needs. Among other changes, the balance of animal production and animal holding in these VRB components may be changed drastically depending on NIH investigators' priorities.

At this writing, the Division-wide Quality and Productivity Improvement Committee has just been established, consisting of one supervisory person and one nonsupervisory person from each branch and the OD. This group will advise the Director, DRS, on initiatives to be undertaken by the Division to maintain its high level of quality and productivity.

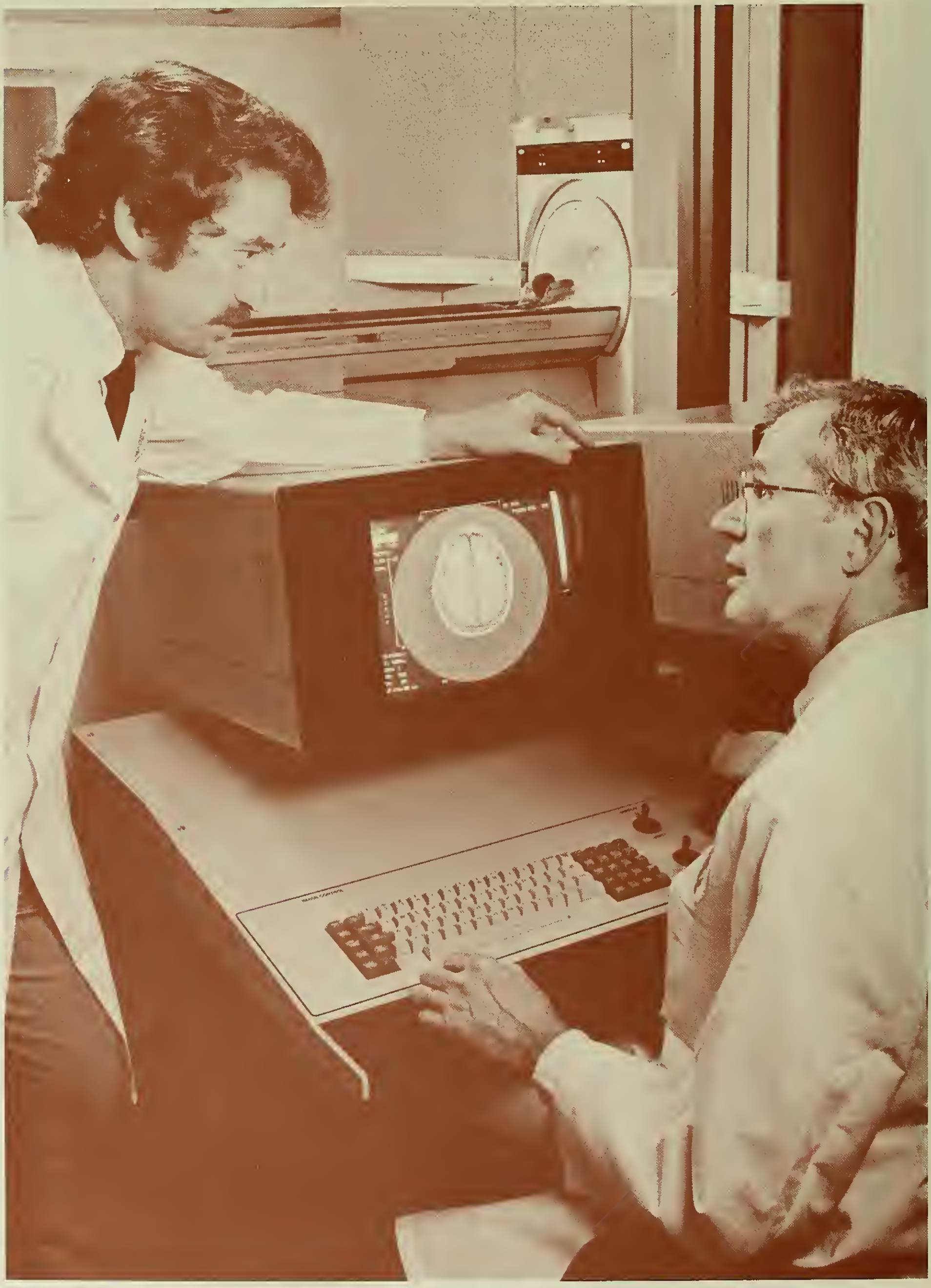
With the beginning of FY 1986, NIH inauguates a "full cost recovery" program

Division of Research Services FY-85 Budget (in thousands of dollars)

Branch	Management	Service & Supply	Total
Veterinary Resources	$5,260	$8,583	$13,843
Biomedical Engineering & Instrumentation	3,261	6,873	10,134
Library	2,893		2,893
Medical Arts & Photography	654	6,360	7,014
Total	$12,068	$21,816	$33,884

whereby many expenses of operating NIH central services were transferred from the Management Fund to rates charged under the Service and Supply Fund (SSF or "revolving" fund). One effect is price increases for many DRS services and products, but not increased expense for the Institute obtaining the service or product, because each Institute's contribution to the Management Fund has been reduced in proportion to the increase in SSF costs. Individual laboratories and sections also have no added expense provided the Institute passes on to them the Management Fund reductions.

In summary, DRS is taking steps to meet the challenge of providing high quality services with fewer resources.



Dr. David Hoult (left), head of BEIB's Nuclear Magnetic Resonance Imaging Group, discusses the Clinical Center's MRI device with Dr. John L. Doppman, Chief of the Clinical Center Diagnostic Radiology Department.

Biomedical Engineering and Instrumentation Branch

Murray Eden, Ph.D., Chief

From the time in the early twentieth century when x-rays first permitted physicians to see glimpses of the anatomy and pathology that lie hidden by a patient's skin, workers in the field of medicine have looked for ways to view the inner anatomy more accurately and in finer detail. The CT scanner, developed a dozen years ago, was an important step forward, because it provided x-ray-generated slices of the anatomy. The radiologist could begin to visualize true three-dimensional anatomy. But CT scans still expose patients to the hazards of x-rays, and its slices can be made in only one plane. Nuclear magnetic resonance imaging, MRI, overcomes both shortcomings; it produces no ionizing radiation, and it can be used to visualize slices in any direction. Moreover, MRI is complementary to x-ray methods; for example, it can distinguish between the brain's gray and white matter—an impossibility by x-ray methods.

MRI Imaging Development in BEIB

Since 1977, when the technique was in its infancy, the Biomedical Engineering and Instrumentation Branch (BEIB), NIH's focal point for engineering and related sciences, has been intimately involved with the development of MRI. In work combining the fields of engineering and physics, BEIB's MRI Group, under Dr. David Hoult, has become internationally recognized for its contributions to the technique's instrumentation. Some of the Group's innovations have become standard features of commercial equipment; one example is the method of selecting an anatomical cross section based upon the formation of magnetic spin echoes. In addition the Group has developed the efficient "rotating frame" method of imaging; an expanded understanding of the origins of noise (unwanted signals) in MRI; a theory of imaging signal-to-noise ratio; and major advances in the design of receiving coils.

BEIB's work on a novel prototype magnet has led to significantly improved understanding of magnetic field homogeneity and to the development of a rigorous method of "homogenizing" irregular magnetic fields by the careful placement of rather small pieces of steel within a magnet's bore. This technique underwent a severe test when the manufacturers of a commercial superconducting magnet for the Department of Radiology, Clinical Center, failed to meet specifications for the magnet's homogeneity. BEIB was able to use its method to improve upon the manufacturer's performance by a factor of fourteen and, thus, exceed the magnet's specifications by a comfortable margin.

How MRI Produces Images

MRI produces images of anatomy by mapping the density of hydrogen (in water and fat) in cross sections of body tissues. It does this by causing the hydrogen nuclei (protons) of the water to interact with magnetic fields applied to the patient. (These fields are typically on the order of 20,000 times as strong as the earth's magnetic field.) The interaction occurs because the protons have both charge and spin and thus are themselves little magnets.

To understand the workings of MRI, it is necessary to know that when a person is placed in a strong magnetic field, his protons (recall, an ensemble of nuclear magnets) tend to align with the field, like compass needles pointing north. From common experience we know that when an ordinary compass needle is flicked, it will swing back and forth, until friction causes it to come to rest pointing north once again. So, too, if a person's protons are "flicked," after they have become aligned with a strong magnetic field, they will oscillate and gradually return to rest in alignment with the field. Because the protons spin, the flicking results in a wobbling motion known as "precession." This is the same motion one will see in a child's spinning top before it falls over.

There is an important relationship between the rate of precession and the strength of the applied field. The number of times per second that the protons precess about the field direction is directly proportional to the strength of the applied field; the stronger the field, the faster the precession. The number of precessions per second, typically millions, is known as the Larmor frequency. It is this proportionality that permits the formation of images.

First, however, we have to "flick" the nuclei. This perturbation of the nuclei is achieved by briefly applying a magnetic field, lasting less than one thousandth of a second, oriented perpendicular to, and rotating about, the main field at approximately the Larmor frequency. To produce this rotating field, alternating current is fed to coils placed about the patient, who is lying within the main magnetic field.

It is in principle a simple matter to detect the precession of the magnetic nuclei. Because they are rotating, the nuclei will induce alternating voltages, albeit weak ones, in receiving coils also placed about the patient. (The receiving coils can be the same ones used to create the perturbation.) This induced voltage is then amplified and recorded in a computer.

It is the proportionality of precession frequency to strength of the applied magnetic field that allows one to obtain information about the spatial distribution of water in tissues and, hence, to produce an image. In MRI there is a gradient in the strength of the main magnetic field; that is, it is somewhat stronger on one side of the patient than on the other. Nuclei in the strong part of the field precess faster and, accordingly, the voltages they induce in the receiving coils are of proportionally higher frequency. With the aid of Fourier analysis, the computer can then determine the strength of the induced voltages at each frequency and, thereby, how many protons are present at each point along the gradient. Admittedly, in the discussion so far no information is obtained from front to back or from top to bottom in the patient, but the experimental details can be modified so that by repeated collection of data the full picture can be obtained.

The characteristic rate of return to alignment of the nuclei after perturbation depends on the chemical environment of the nuclei—just as the amount of friction in a compass needle's bearing determines how quickly it returns to rest. Measurement of this phenomenon in the body by MRI allows inferences about the patient's biochemical and physiological state.

BEIB in FY 1985

BEIB has also been busy fulfilling its commitment to provide the NIH research community with a broad range of scientific and engineering expertise. For example, BEIB has collaborated in more than 200 projects to produce advanced instrumentation, models, methods, and techniques dedicated to the acquisition of biomedical information previously unavailable to NIH's scientists.

This year, as in the past, members of BEIB have been honored for their achievements. For example, two staff members received an award for best paper presented at the annual meeting of the Electron Microscopy Society of America. In addition, one of these authors received the Society's Burton Medal. Another staff member was honored with the Centennial Medal of The Institute of Electrical and Electronics Engineers (IEEE). Still another won an NIH Director's Award and the Gold Medal of the Society of Magnetic Resonance in Medicine.

The staff of more than 40 professional physical scientists and engineers and 80 technical support personnel responded to over 2500 requests for the fabrication and modification of laboratory devices and made another 9000 repairs and minor changes of scientific equipment.

BEIB's professional staff functions within four sections and the Office of the Chief. Here is a brief description of their activities in FY 1985.

Applied Clinical Engineering Section (ACES)

The ACES continues to support a variety of biomedical research throughout the NIH. The majority of its collaborations are located in the Clinical Center (CC), however, and relate directly to patient care. The remaining research projects are in areas where the Section has a particular expertise.

For example, the ACES has been working closely with the Clinical Pathology Branch of the CC on flow cytometry and cell kinetics. The Section's contributions have included improving the optics and flow cells of flow-cytometry equipment and developing novel techniques of mathematical filtering and analysis.

The ACES has also worked closely with the Surgery Branch of the National Cancer Institute (NCI) in an effort to understand the mechanisms of postoperative recovery. The Section's initial contribution has been to an improved understanding of wound healing. Cancer patients are at high risk for postoperative complications of surgical incisions. Our studies have shown that the primary hindrance to wound healing is the administration of chemotherapeutic agents. Data from animal models demonstrate that the suspension of chemotherapy for three days after surgery is sufficient to permit normal incisional healing.

The ACES is also collaborating on a project designed to enhance understanding of the pathophysiology of cachexia in patients with sarcoma. So far the studies demonstrate that patients with metastatic disease have levels of energy expenditure greater than those of controls. To measure the energy that patients expend, the patients are semi-encapsulated in a metabolic chamber that uses a mass spectrometer to compare the content of air leaving the chamber to that entering the chamber.

The ACES assists operating room and intensive care unit clinicians to evaluate newly available equipment. Recently, for example, disposable pressure transducers became available as an alternative to traditional, labor-intensive, reusable pressure transducers. The ACES tested ten of each manufacturer's devices for frequency response, drift, linearity, and safety. Additionally, the ACES evaluated other critical patient-care devices, such as defibrillators and intravenous infusion pumps. The ACES and the Clinical Center Instrumentation Section (CCIS) are also responsible for the ongoing semiannual electrical safety inspection of all equipment used in the Clinical Center.

The Section has also been active in developing instrumentation to study rheological properties of red blood cells. In particular, it has been developing novel devices to study the effects of environmental changes on red blood cells during filtration. (The filtration system is being used to assess the ability of conditioned cells to deform during passage through the microcirculation.)

Outside the Clinical Center, the members of the ACES serve as specialists in microcalorimetry, a field that requires measurement of heats of chemical reactions that produce only microjoules of energy. The ACES has also transferred this technology to the field of x-ray diffraction; the Section developed a hypobaric x-ray specimen chamber, using the same solid-state heat pumps and electronic circuitry used in the microcalorimeter to provide precise temperature control of specimens to be analyzed by x-ray diffraction.

In addition, the ACES is providing technical assistance to scientists in NINCDS, who are studying intracerebral regulatory mechanisms, particularly cortical blood flow and metabolism. Techniques being used include two-channel reflectance spectrophotometry and fluorimetry through optic fibers. These studies will attempt to answer questions concerning cortical metabolic and hemodynamic disturbances seen in certain clinical disorders, such as Alzheimer's and Parkinson's diseases.

Chemical Engineering Section (ChES)

The Chemical Engineering Section is a resource at NIH for applications of the science and technology of chemical engineering to problems in biomedical research. The Section has active programs in such areas as transport phenomena, pharmacokinetics, fluid mechanics, biomaterials, and instrumentation.

The Section has, for example, applied transport theory to a number of physiological and pharmacological problems. Diabetic retinopathy is a major cause of blindness, and it has been reported to be associated with a greatly increased leakiness of the blood-retinal barrier. It would be of great value to have a simple technique that would identify the problem early in its development and could be used to assess the results of therapy. Vitreous fluorophotometry has been used to measure the distribution of the fluorescent dye fluorescein in the human eye after the dye is injected into the blood. The analysis of such data has been placed on a more rigorous basis by the development of a mathematical model that includes the characteristics of the blood-retinal barrier and diffusion through the vitreous.

In another application of transport theory, the distribution of platinum derived from a platinum-containing anticancer drug (DDP) has been analyzed, based on data derived from long-term infusion of the substance into the brains of rats. The section has developed a diffusion-permeation-reaction model that provides estimates of the rate constant for reaction of the drug in brain tissue, the diffusivity of the drug in brain, and the capillary permeability. These parameters are important for the design and analysis of strategies for using localized infusions of DDP to treat brain tumors. For example, the parameters can be used to calculate drug distribution near sites of infusion, concentration profiles associated with drug administration to the cerebrospinal fluid, and the effect of alteration of capillary permeability by pharmacologic or pathologic processes.

The limited therapeutic index of most anticancer drugs has prompted many investigators to consider regional drug delivery. One of the most common of these is infusion into the artery supplying blood to the tumor-bearing region. The pharmacokinetic advantage of intra-arterial drug administration can be increased if venous blood from the infused region is processed in an extracorporeal device to remove at least part of the drug before if reaches the rest of the body. The Section developed the phamacokinetic theory for this procedure and conducted clinical trials of hemodialysis to remove DDP infused into the internal carotid artery. A study involving four patients with brain tumors has shown that the systemic exposure was reduced by 49 to 74 percent. Additional studies are under way with twice the standard dose of drug combined with dye infusion to confirm that the proper choice has been made of vessels for drainage.

Work continues in the Section on experimental fluid mechanics, including studies of the extent to which drugs mix with blood during infusion from small catheters. Experiments performed using a model of the human carotid artery have demonstrated that streaming (non-mixing) of the infusate can occur at infusion rates comparable to those commonly used during infusions into the carotid arteries for treatment of brain tumors. Such streaming results in nonuniform distribution of a drug in tissues and suggests an explanation for the varied success and sporadic toxicity of this form of treatment. The studies have shown that mixing can be enhanced by using higher infusion rates and other techniques. *In vivo* studies using fast and slow infusions of a radioactive tracer into the carotid arteries of monkeys have corroborated the *in vitro* results. Concentration ratios of tracer as high as 13 to one were detected by quantitative autoradiography within those sections of monkey brain served by the middle cerebral artery. This suggests that future protocols requiring intra-arterial infusions use methods to enhance mixing, such as higher infusion rates or specially designed catheters.

In this connection the Section has developed a double-lumen jet catheter. Contrast agent or other liquid can be pumped through one or both of the retrograde jets at the catheter's tip. This provides a radiologist or other physician the ability to literally steer the catheter through twisting and branching arterial networks. A significant additional advantage is that drug infused at adequate flow rates through the jets distributes quite uniformly in distal arterial branches in the *in vitro* model mentioned above.

Measurement of the oxygen partial pressure ($p0^2$) in blood and tissue is an important requirement in a variety of research and clinical applications. For this purpose the Section has developed a fiber-optic probe that is small, flexible, safe and—potentially—quite inexpensive. The probe is based upon the principle of fluorescence quenching and, thus, provides a reversible measure of blood and tissue $p0^2$. The original design used two fibers, one to carry light from a source to the probe and one to carry the signal to a detector. The instrument design and probe construction were changed to a single-fiber version for simplicity of construction, improved performance, and compactness. In addition, the Section developed a method of incorporating the probe within a small-gauge needle, facilitating its insertion into tissues.

Electrical and Electronic Engineering Section (EEES)

The Electrical and Electronic Engineering Section (EEES) continued its program of applying the power of modern electronic technology to the needs of biomedical research. The interaction of several disciplines is strikingly evident in the collaboration of EEES staff with members of the Radiation Oncology Branch, NCI, to advance photoradiation therapy (PRT) for the treatment of cancer. PRT is creating intense interest because its ratio of toxicity to malignant cells vs. normal cells apparently can be as high as 10:1, whereas methods such as chemotherapy and hyperthermia are often limited to a ratio of 2:1 or less. This specificity results from one of the remarkable properties of hematoporphyrin derivative (HPD), which is injected into the region of concern. The HPD is taken up by all of the cells, but is quite thoroughly eliminated by normal cells within a few hours. On the other hand, its elimination by malignant cells is much slower. A second property of HPD can then be exploited to destroy the malignant cells. When illuminated by visible light, HPD converts oxygen in its vicinity to the highly toxic singlet state.

Delivering the light is not as simple as it might sound, because of the highly scattering character of most tissues. For small tumors a fiber-optic probe can be used, and 100 percent cure rates have been achieved in a mouse model by this method. When the malignancy has spread, however, it is difficult to deliver sufficient radiant energy to every element of the required volume, and the EES is now working on this problem. Effort is also being directed to the dosimetry of singlet oxygen, which is necessary to put the technique on a sound scientific basis and to facilitate its further development. The fluorescence characteristics of singlet oxygen in various environments, as well as HPD and the usual background fluorescence, are being evaluated as a basis for developing a time or frequency domain fluorescence assay.

Laser angioplasty is another major electro-optic project in collaboration with researchers in the Surgery and Cardiology Branches of NHLBI. This project envisages the use of radiant energy from a laser to remove plaque deposits from coronary arteries as an alternative to surgical intervention. Almost all laser surgery to date has depended on conversion of the radiant energy to thermal energy, which then vaporizes or otherwise alters material at the target site. This blasting approach would probably be too damaging to the arterial wall, however, so photochemical decomposition of the deposits is being explored. NASA Goddard and the Naval Research Laboratory have collaborated in the evaluation of various types of lasers and delivery systems, and, as a result, an excimer laser has been ordered. Substantial effort has been directed to development of the complex catheter needed for viewing, flushing, and excitation, and to the video system needed for display and storage of information. The apparatus has been tested on dead and live animals and on humans.

The Section is devoting considerable effort to applications of the laser-doppler blood flow meter, which was developed earlier. This work has received national attention for studies of vascular dynamics in patients with sickle cell disease. Another project in progress is a fluorometer intended to exploit the potential of new rare-earth chelate probes with long decay time constants to overcome the effects of background fluorescence, thus providing an alternative to radio-assay techniques for low level measurements. This work is in collaboration with the Laboratory of Technical Development, NHLBI, and the Centers for Disease Control, Atlanta.

The use of magnetoencephalography (MEG) for the localization of epileptic foci is being actively pursued in collaboration with the Division of Computer Research and Technology (DCRT) and the Medical Neurology Branch, NINCDS. Considerable patient-derived data were taken with a single-channel MEG system and processed manually; this led to significant progress in the areas of modelling and signal processing. A room with low extraneous magnetic fields was obtained for development as an MEG lab, and a seven channel detector system with associated computerized data acquisition and processing capabilities was specified and ordered. Methods to use EEG data to enhance the interpretation of MEG data were developed.

A large number of smaller projects accounted to about half of the Section's efforts in fields as diverse as low light level video, special-purpose nuclear magnetic resonance systems, biotelemetry, microprocessor and computer-based instrumentation, imaging systems, vocalization analysis, and ultraminiaturization of equipment.

Section capabilities were augmented by additional software for the Section's personal-computer-based engineering work station, and planning is under way to develop capability to use field-programmable logic devices. These devices combine programmable read-only memory with other features so that devices equivalent to custom-made integrated circuits can be quickly developed in the field with a small PC-based facility. They should be ideal for the many rush, one-of-a-kind jobs that constitute a large part of the Section's workload.

Mechanical Engineering Section (MES)

The Mechanical Engineering Section conducted a wide diversity of collaborations with scientists in NIH's intramural research program involving analytical and experimental studies and the development of specialized instrumentation. For example, in continuing work with the Hypertension-Endocrine Branch of NHLBI, the MES refined a mathemathical model of pulse-wave propagation in the brachial artery through optimization of the model's parameters. Preliminary ultrasonic measurements of velocity and brachial diameter carried out by the Section have now confirmed some of the predictions of the model and have led to increased understanding of the mechanics of vasoactive responses in normal and hypertensive subjects.

The Section has also begun a research collaboration on cardiovascular dynamics with several INSERM laboratories in France. Specific areas under investigation are myocardial blood flow, ultrasonic backscatter from the myocardium, myocardial and ventricular mechanics, and wave propagation in arteries. The intent of this work is to improve the basic understanding of each of these topics through measurements on animals and humans and the use of mathematical and physical models.

A multi-year effort in collaboration with the Radiation Oncology Branch, NCI, is making substantial progress in the development of equipment and protocols for regional, radiofrequency-induced hyperthermia, used as an adjunctive treatment for cancer. The goal is to gain better understanding of the electromagnetic and thermal processes in tissues and to improve the efficiency of systems under development. In order to predict the patterns of energy deposition and the resulting temperature distribution within tissues, the Section has employed a combination of techniques using large-scale computerized electromagnetic "block models" and thermal "finite-difference models." In addition the Section has used electric field temperature probes in conjunction with various phantoms to measure experimentally the actual electromagnetic and thermal fields produced by different applicators.

The Section has shown that some hyperthermia protocols, developed elsewhere, can cause undesirable heating outside of an intended region in a patient's body and that, under certain circumstances, medical personnel using the equipment might inadvertently absorb as much energy as the patient being treated. Conversely, the Section has shown that other protocols should be effective in heating previously untreatable areas involving the long bones of the extremities. The Section anticipates that within the next year the integration of these experimental with analytical efforts will culminate in the development of a clinical system, using computer-controlled protocols.

The Section continued its innovations in a variety of areas of bioinstrumentation, including optical sensors to automate the measurement of cell concentrations in culture media and fermenters, thereby greatly reducing time-consuming manipulations by researchers; fiber-optic probes for assessing the viability of teeth and the presence of caries; clinical methods for using ultrasound to measure arterial wave speed, as well as phasic velocity and dilation; relatively inexpensive equipment for molecular biologics, such as an automated cell colony scanner and an inexpensive automated single-cell distribution system; a portable system to quantify "circling" behavior in ambulatory psychiatric patients; and an apparatus to produce precise shear fields in an Electronic Spin Resonance (ESR) system. The Section has also embarked on a study of novel extrusion techniques for small-diameter polymer tubing to enhance the capabilities of previously developed everting catheters.

The Section is continuing to develop a theoretical model of cochlear processing in collaboration with the Mathematical Research Branch, NIADDK. The model incorporates basilar membrane motion, fluid-cilia coupling, and hair-cell transduction. The Section has computed the model's responses to pure tones and is now studying more complex inputs.

Analytical Methods Group

Members of the Analytical Methods Group continue to develop advanced physico-chemical methods for identifying, characterizing, and quantitating a large variety of constituents making up complex biochemical and biological systems. Recent work has included the development of techniques to fractionate complex chemical species of biologically important elements using chromatographic methods, to characterize them by various physicochemical methods, and to quantify the species using electrothermal atomization and atomic absorption spectrophotometry. The Group can also apply the techniques of neutron activation analysis when it is necessary to use the senstivity of this technique and when the elements sought have suitable characteristics.

This work has emphasized quantitation of complex chemical species of metallic elements present in trace concentrations. This frequently presents an unusually difficult challenge for the analyst, because the quantity of sample itself is very small.

The principal projects are conducted in collaboration with investigators in the National Institute of Dental Research (NIDR), National Institute of Mental Health (NIMH), National Institute on Alcohol Abuse and Alcoholism (NIAAA), NCI, and NHLBI.

The Group has been studying the quantitative distribution of chemical species of cis-platin, a drug used in cancer treatment, as a function of time and in different chemical environments. These developments have required devising new, more refined methods of separation coupled with development of electrochemical detection methods offering the high sensitivity required. Transformations among various species studied occur slowly; clinical oncologists may be able to use this behavior to obtain reduced toxic effects of the drug.

Collaboration with NIMH and NIAAA is continuing on the determination of levels of the order of nanograms per gram of vanadium in the blood and cerebrospinal fluid of normal volunteers and patients with manic-depressive behavior.

Further, in collaboration with researchers at the Oscar Lambret Cancer Treatment Center in northern France, the Group is characterizing the kinetics and uptake of trace levels of platinum complexes in cultures of human respiratory tract tumors. In some cases, where local concentrations are sufficiently high, use of a microprobe has permitted analysis of elements localized in subcellular structures. This work has been conducted in collaboration with investigators in NCI, NHLBI, NIMH, and NIAAA.

A major accomplishment in this year was development of a data system based on the IBM PC-XT. The system was designed to control the quadrupole mass spectrometer of the SEMS system and to scan the energy of secondary ions to obtain energy distributions. We have initiated a systematic study of various organic ions in relation to the different experimental conditions in liquid SIMS experiments. This work will expand into studies of various amino acids, as well as other biologically important compounds. The development of the data processing system is continuing with the goal of producing images of biological specimens by use of the SEMS system. As in the past, this work is conducted in collaboration with the NHLBI and NIMH.

Research in the area of the physical chemistry of biological macromolecules has included collaborations with several institutes. For example a scientific report on inter-photoreceptor retinoid-binding protein has been published jointly with NEI. Studies on the thermodynamics of the association of the subunit chains of the toxic protein ricin and the relationship of this association to cellular toxicity have been completed with NINCDS and submitted for publication. New studies on ricin-antibody interactions are under way. Initial studies on heparin sulfate proteoglycans from tumor basement membrane have been completed and submitted for joint publication with

NIDR. Current studies in this latter area deal with the extent of heterogeneity of these molecules and a study of their interactions with structural proteins, such as laminin and type-4 collagen. Studies on the association of Factor XIII from plasma and platelets with fibrinogen have been completed; current work is directed toward studies of the association of plasminogen with the D and E fragments of fibrinogen and studies on the interaction of fibrinogen with other proteins involved in blood clotting and fibrinolysis. Studies in conjunction with NINCDS on the binding of human chorionic gonadotropin to cell surface receptors and studies in conjunction with NICHD on the association of HCG subunit chains have been initiated. Studies on improvement in instrumentation and methodology of analytical ultracentrifugation are continuing, including progress in the mathematical modelling used for data analysis.

Electron Beam Imaging and Microspectroscopy Group

The group has been expanding the capabilities of its computer-controlled analytical electron microscope and applying this technology to a number of collaborative projects. A greatly improved electron energy loss spectrometer has been recently added to the instrumentation, and for the first time this has permitted simultaneous acquisition of element-specific electron energy loss and energy dispersive x-ray signals, as well as the dark-field elastic signal which is characteristic of sample morphology. Further developments have also taken place in the processing of spectra and elemental images to improve quantitation procedures.

In collaboration with the Laboratory of Cell Biology and Genetics, NIADDK, the Group has been determining the composition of secretory granules in adrenal chromaffin cells. Samples were prepared by rapid freezing and ultracryomicrotomy. Ionic concentrations of potassium, calcium, sodium, and chlorine were measured and compared with existing data from isolated chromaffin granules. Some information about the concentration of proteins, nucleotides, and catecholamines was also obtained. These data are relevant to understanding the physiology of a resting chromaffin cell and the changes that occur when it is stimulated.

In collaboration with the Laboratory of Neurobiology, NINCDS, the Group has been determining the elemental distribution of calcium and potassium in rapidly-frozen, cryosectioned mouse cerebellar cortex. Of particular interest was the identification of intracellular calcium stores possibly localized in the endoplasmic reticulum of Purkinje cell spines in repetitively-stimulated cortex. Calcium stores were not evident in the presynaptic nerve terminals of resting or stimulated cells. The results suggest fundamental differences between presynaptic and postsynaptic nerve endings with regard to the mechanisms of calcium mobilization and transport.

In collaboration with the Pulmonary Branch, NHLBI, the Group has obtained electron energy loss (EELS) and energy dispersive x-ray (EDXS) spectral maps of elemental distributions in macrophages obtained by broncho-alveolar lavage from patients with silicosis, asbestosis, and coal miners' lung disease. Data were also obtained from alveolar macrophages in lung biopsies. The study is being used to correlate disease with the incidence of inclusions in the macrophages.

A study has been made in collaboration with researchers from the Biozentrum, University of Basel, Switzerland, to investigate the feasibility of low-dose, high-resolution electron energy loss mapping of two-dimensional membrane crystals. Experimental measurements and theoretical predictions show that averaging procedures over ten thousand unit cells should provide the distribution of phosphorous and nitrogen in the lipid and protein components respectively at a dose of about ten electrons per square angstrom.

The instrumentation of the Group also includes a 50 keV electron beam microanalyzer, which is connected to the Group's laboratory computer. Using this device, the Group has collaborated with NINCDS to localize and image aluminum, silicon, magnesium, and calcium in the hippocampal region of brains of victims of Parkinsonian dementia, ALS, and Alzheimer's Disease. This effort has been highly successful: the group has produced clearly resolved images of these elements in neurons and axons. In addition, we have collaborated with the Clinical Pathology Department, CC, in an effort to quantitate and image the magnesium content of individual lymphocytes.

Scientific Equipment Services

Scientific Equipment Services (SES) provides instrument fabrication, repair, and rental services to the NIH scientific community. During the past year, SES has begun a program to analyze its operation and to develop initiatives that will increase both the range and quality of services it offers while reducing the cost of these services. The following are examples of some of the initiatives brought about through this program:

- A “loaner” program to begin in fiscal year 1986 will make selected equipment available to researchers while their equipment is being repaired.
- A new computerized job-control system will permit supervisors to expedite work requests and keep requesters informed about the status of their requests, as well as reducing the cost of providing these services.
- Increased procurement authority for SES’s procurement department and the stocking of frequently-used circuit boards will reduce turnaround time.
- A new computerized system for monitoring contract repairs has resulted in more efficient management of these jobs.

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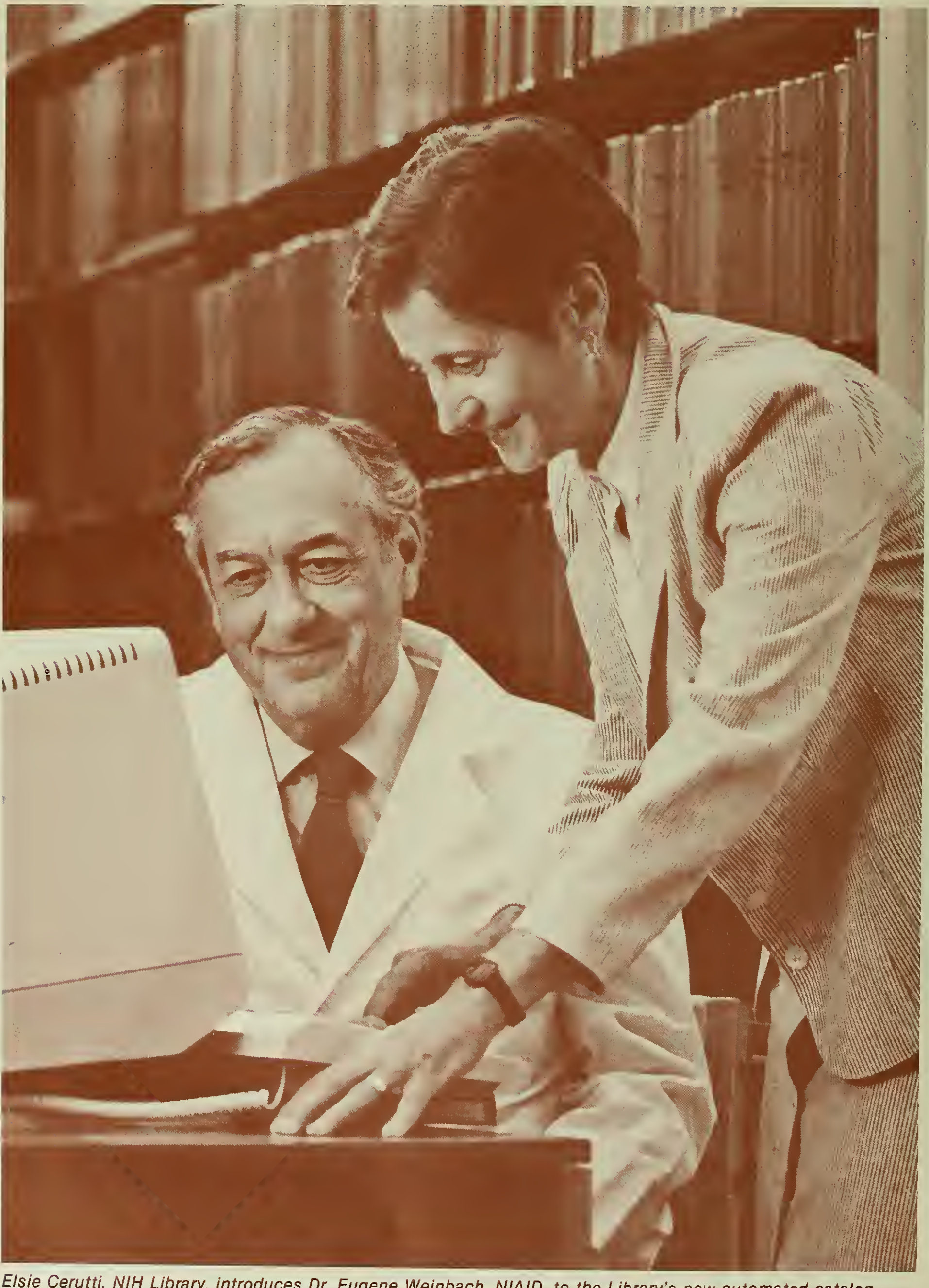

Elsie Cerutti, NIH Library, introduces Dr. Eugene Weinbach, NIAID, to the Library's new automated catalog.

Library Branch

Carolyn Brown, Chief

The significant event of the year for the Library Branch was the unveiling of the automated online catalog and circulation system. In preparation for this event, several years of staff work were used to develop machine-readable records, place barcodes on library materials, and correct the bibliographic file. During March 1985, the Library staff prepared new Library cards by placing barcodes on the NIH identification cards of eligible NIH borrowers. In April 1985, the circulation system and automated catalog became operational. The Library has chosen a mix of keyboard and touch terminals for public access to the system in the Library. Recently the Library began experimenting with remote access to the system, allowing dial-in availability to several NIH staff in a pilot project.

To smooth the transition from card catalog to the automated system for Library users, the staff of the Reference and Bibliographic Services Unit wrote a brief guide on use of the keyboard and touch terminals. If users appeared to have difficulties, Library staff members were available from 8:30 a.m. to 5 p.m., Monday through Friday to give individual instruction. The Technical Services Section staff who usually work behind the scenes acquiring and processing Library materials joined public service staff in this undertaking. A weekly one-hour course was also initiated in late summer to give more detailed instruction to NIH Library users.

Library Instruction

Assuming an educational role, the Reference and Bibliographic Services Section initiated a course, "MEDLINE for the Health Professional," which has been received with enthusiasm by the NIH staff. As an adjunct, experienced search staff are assigned to give advice to NIH staff on individual search problems. Increased assistance to users who perform their own bibliographic searching is a trend which is expected to continue. The search service has not experienced a decrease in search requests as a result of users doing their own searching. The questions to the search service, however, appear to be becoming more complex, leading to the conclusion that users do their own easy searches but refer the difficult problems to the Library's specialists. After a high growth period in 1982, the number of searches has remained at approximately 8500 searches per year and current awareness searches at approximately 350 profiles per year.

Along with guides to searching the online catalogs, the Library published the second edition of the brochure "NIH Library . . . in Brief." The guide is given to new Library registrants and to NIH staff who take the Wednesday Library tour.

Collection Review

An organized review of Library journal subscriptions is being conducted by the Reference and Bibliographic Services Section in conjunction with groups of specialists chosen from the NIH research community. To date 648 journal subscriptions from a total of 3,470 have been reviewed; of those reviewed, 59 (9 percent of the reviewed titles) will be cancelled in calendar year 1986. In addition to the review by NIH research staff, the Library staff is gathering photocopy usage data and circulation data for another 320 journal subscriptions which include second copy subscriptions and titles about which the review groups did not agree.

Benefits of Automation

The collection of usage data is a sideline benefit of the new automated catalog, which tabulates data on the number of times a journal or book is photocopied or borrowed. Projected upgrading of software to the automated system, to provide not only circulation usage figures but in-house usage of the collection, will be a powerful Library management tool for refining the collection and acquiring new publications. Additional subscriptions to several of the most popular journals are a direct result of having data on the number of times a journal is used in the self-service photocopy area.

The linking/labeling of all Library materials during the summer of 1984 in preparation for the online catalog also provided the Library with its first inventory of the entire collection. A computer-generated list of books missing from the shelves is being reviewed to ascertain current need for the material. Staff are ordering replacement copies of some and deleting records for others.

Inprovement of Service

The FY 1984 reorganization of the management of photocopy requests provided a 24-hour turnaround time when no situation was encountered in which the requested book or journal was already in use. The new popularity of the service is an indication of improved management. Numbers of requests increased 82 percent in 1985 over 1984. The processing time has been consistently good: 71 percent of all requests are completed by day 2 and 87 percent by day 3.

In addition to the growth in providing copies of material in our collection, the work of the Interlibrary Loan Unit also increased. This year we borrowed 34 percent more than last year. An analysis showed that 80 percent of the requests were for books not owned by the Library, primarily in philosophy and psychology; 20 percent of the requests were for items missing from the collection, particularly in the fields of physiology and internal medicine.

Through the year users faced delays in obtaining needed material because many journals were at the binder for extended periods. This problem appears to be solved with the selection of a new binder for the coming year, one whose past performance indicates reliability and speed of handling.

Using the same number of FTE's, the Translation Unit had an 11 percent increase in total jobs completed in FY 1985 over FY 1984, as well as a 20 percent increase in total words translated.

Renovation

Concourse renovation in the Clinical Center necessitated change in space allocations for the Library's reading and stack areas on the B1 level. Space previously occupied by the Medical Arts and Photography Branch along the west wall was provided to the Library in exchange for an area approximately the same size along the east wall. The new area was completed in June, and the lower level collection of abstracts and indexes was moved. Also during this period the Photocopy Service area was completely renovated to provide more efficient work areas and space for additional equipment. Lighting, temperature control, and ventilation were much improved.

Publications

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Services of the NIH Library

The NIH Library offers a full array of services to assist scientific investigators in their work. They include:

- **Computer Bibliographic Searches** - Technical specialists perform computerized literature searches and compile bibliographies upon request. The staff is experienced in retrieving citations and abstracts from some 155 scientific databases. (Request from Reference and Bibliographic Services.)
- **Current Awareness Service** - The Library's Selective Dissemination of Information (SDI) program provides users with regular computer updates on new literature in the biological and medical sciences. (Request from Reference and Bibliographic Services.)
- **Reference Services** - Reference librarians not only answer reference questions on site or by telephone (496-2184), but also advise users of other library services that may meet their needs.
- **Photocopying** - Copy machines are available to users in a self-service area. (Photocopy Service, lower level.) The Library also will locate and copy articles upon request. (Request form at Circulation Desk.)
- **Microfilm and Microfiche** - Many journals are also kept in microform. Most are backfiles of important titles, acquired in order to save space. Reader-printers are located nearby.
- **Circulation** - Books other than reference works and noncirculating reserve items can be checked out. Second copies of some of the most popular journals are also available for circulation.
- **Interlibrary loans** - Research publications not in the collection can be obtained from other libraries. Photocopies of journal articles obtained from the National Library of Medicine are usually provided in one to two workdays.
- **Translations** - Foreign-language scientific materials are translated upon request from NIH staff. All translations are made available to other users.
- **Stacks Service** - Library staff will search for any volume a user cannot find on the shelves. (Request form at Circulation Desk.)
- **Publications** - "Recent Additions to the NIH Library" is available monthly in printed form and on the NIH WYLBUR computer system. "Current and Noncurrent Journals: NIH Library" is published biannually. Copies are available from the Circulation Desk.
- **Library Tours** - A tour providing an overview of NIH Library services and policies is available every Wednesday at 2 p.m., beginning from the Reference Assistance Desk.
- **Carrels** - Private study carrels are available on a limited, first-come basis. (Circulation Unit.)
- **Instruction** - Instruction on the use of the NIH Library and the automated catalog is offered periodically. "MEDLINE for the Health Professional" is taught monthly. (Further information available from Reference and Bibliographic Services.)
- **NIH Library . . . in Brief** - This eight-page Library guide is available upon request at the Circulation Desk.

Reduce Your Risk of Cancer By Making Healthy Choices.
NCI Cancer Information Publications

NIH Institutes provide information to the public through exhibits created by the teamwork of Institute representatives, MAPB staff, and contractors.

Medical Arts and Photography Branch

Ronald B. Winterrowd, Chief

The Medical Arts and Photography Branch (MAPB) provides multi-media visual communication services to the NIH community, documenting medical research programs, accomplishments, and scientific data through photographs and graphic illustrations for publication and for presentation at conferences. MAPB provides numerous services to meet all information needs.

The Branch's staff of professional artists, photographers, and other specialists have extensive expertise in converting data into effective presentations. They are highly skilled in meeting the needs of scientists for graphic presentation, medical arts, and still and motion picture photography, including photomacrography and photomicrography. Services included design and production of publications; preparation of slides, vugraphs, and other projected visual aids; animation artwork; exhibit design; statistical drafting; display charts; posters; medical illustrations; and three-dimensional models.

The philosophy of the Branch is to provide high quality professional services competitive in cost with commercially obtainable services. On contracted work, the staff works closely with vendors of design, graphic, and photographic services to ensure that MAPB's quality standards are maintained.

During FY 1985, an internal reorganization was accomplished within MAPB. Organizational components now consist of the Design Section, Graphics Section, Photography Section, and Medical Illustration Section. In addition, motion picture services and special projects were consolidated as the Motion Picture and Special Events Unit. The new organizational structure improves overall management effectiveness, removes an unnecessary management level, and gives recognition and identity to the Branch's distinctly separate major functions.

The Branch continued sending a team of staff members to NIH laboratories and other units to explain its services, inform users of cost-saving measures, and obtain suggestions on how services can be improved. Units in every Bureau, Institute, and Division have been visited, and MAPB wishes to remind its users that staff will gladly visit any NIH unit, no matter how small, for an information exchange.

Demand for MAPB services continues to be constant and heavy. In order to accommodate the volume and diversity of services requested by the NIH community, MAPB utilizes the services of a wide variety of small and minority businesses in the Washington metropolitan area. In order to reduce costs to the requestor, MAPB requires competition among qualified vendors for many jobs, and daily bid sessions are held for all graphics job requests.

Photography Section

The Photography Section's requests for laboratory services increased by 15.3 percent during the year. Photographic support services, Photomicrography, Photomacrography, Clinical Photography, and Photographic Technical Information increased by 18.7 percent.

The Photomacrographic Unit installed a Reprostar Ultraviolet Lighting System for making high quality photographs of thin-layer chromatography plates and electrophoresis gels. Wave lengths of 240 nm, 300 nm and 366 nm are possible with either transmitted or reflected light. This unit is superior to any lighting unit previously at NIH and makes very high quality ultraviolet photography available to NIH investigators.

The Photography Section continues to supplement in-house photographic laboratory services by obtaining services of private photographic facilities in the Washington, D.C. area.

Design Section

This Section is composed of a group of professionally trained, highly skilled and experienced designers. Many have won awards in local, national, and international art competitions. The Section provides the NIH community with design services both for scientific presentations and public information. This includes publications, posters, editorial and technical illustrations, and slide shows, as well as design and preparation of support materials for various conferences organized at NIH. In FY 1985, the Design Section continued to experience an increased demand for services. As the work load increased, and the FTEs were reduced, more job requests than in previous years were coordinated with local private companies. High productivity of in-house personnel made it possible to lower the hourly rate by 6 percent in FY 1985, while maintaining the reputation for high quality enjoyed by the Design Section.

Graphics Section

This Section is composed of professionally trained, highly skilled and experienced illustrators and visual information specialists. The Section provides the NIH scientific community with graphic art for scientific presentations and public information; this includes illustrations, posters, charts, graphs, tables, computer generated graphics, typesetting, and slides, as well as the design and preparation of support materials for various conferences organized at NIH. The volume of requests for service continues to increase with FY 1985 total production units projected at 235,000, a 10 percent increase over FY 1984. The Graphics Section continues its efforts to reduce costs, and daily bid sessions are held with various vendors of the area to keep costs down.

This Section purchased new equipment which will increase in-house capabilities. Requesters who use word processors will be able to send data via telephone to the new equipment for type specifications, design, and layout. The Section expects to purchase a graphics terminal in FY 1986; it will also do charts and graphs.

Motion Picture and Special Events Unit

The Motion Picture and Special Events Unit was formed early in FY 1985 and has a staff of five professionals. The functions of the new unit include motion picture services of cinematography, sound recordings, editing, and related laboratory services; scientific videotaping services; and all special events including poster presentations, slide shows, exhibits, congressional and VIP presentations, Medicine for the Layman lectures, signage system design and production, and other special requests.

Medical Illustration Section

The Medical Illustration Section produced a wide variety of black-and-white and color medical illustrations and diagrams of surgical, gross pathological, ophthalmological, biological, and dental subjects. Three-dimensional medical models, moulages, and related fabrication were also provided for presentations, exhibits, and patient and physician education. Medical illustration services are requested to describe complex medical and surgical procedures. Long hours of surgical observation, research, and planning are usually necessary before initiation of many projects; extensive knowledge of human anatomy and of artistic techniques and applications is required.

Outlook for FY 1986

FY 1986 will be a challenging year for MAPB because of the conversion of all MAPB Management Fund functions to the Service and Supply Fund, the implementation of the full cost recovery initiative, and reduction of FTEs. Every effort will be made to reduce the cost impact of these changes upon MAPB requestors through continued competition among MAPB vendors, increased in-house productivity, and informing clients of ways they can reduce costs for job requests.

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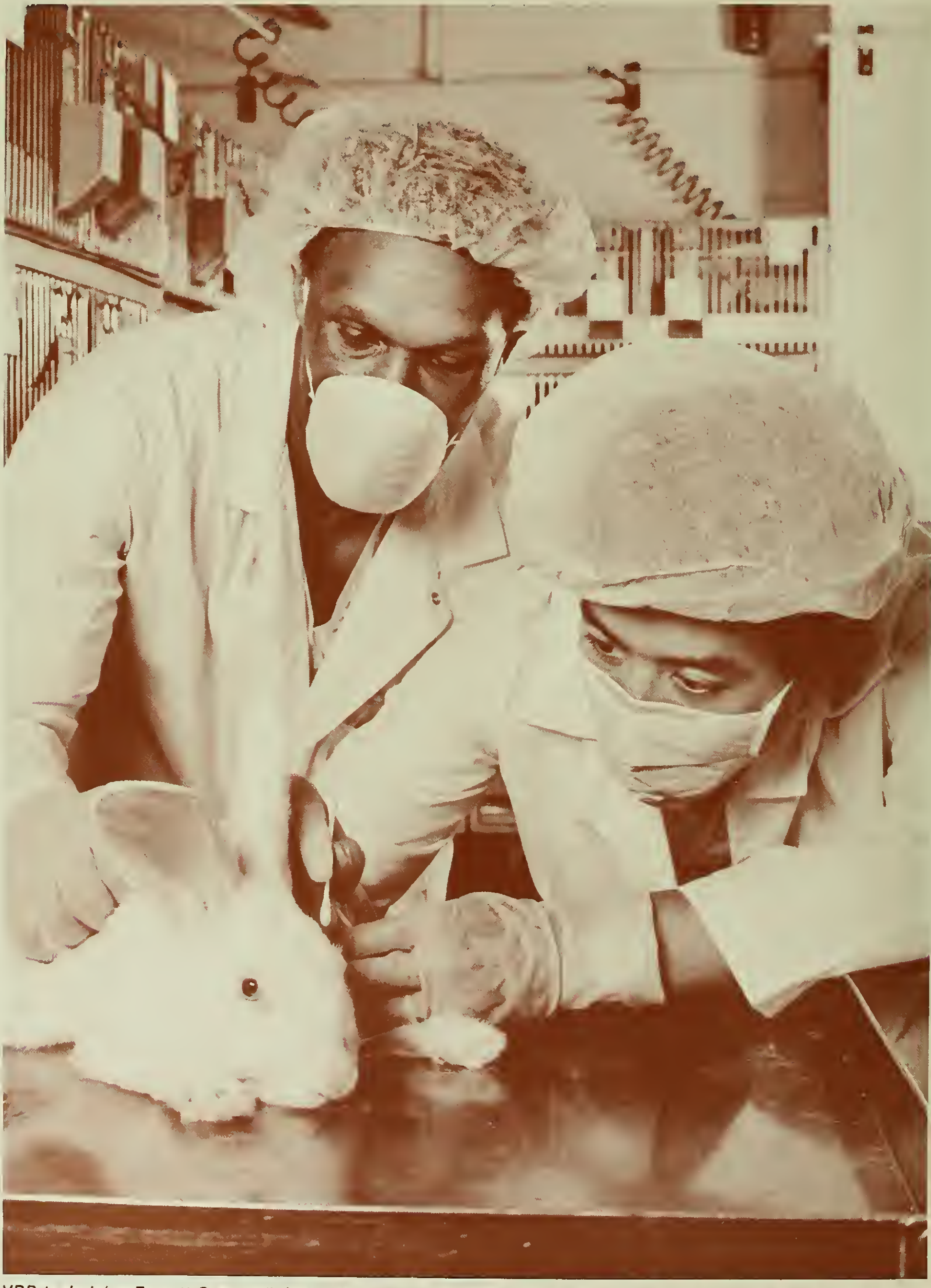
Wilcox, M.A. and Bartner, H.C.: A teaching model for nasal irrigation. *J. Biocommun.* 13-15, 1984.



VRB technician Everett Garnett (left) assists NHLBI scientist Dr. David Lu with animal studies at the Research Support Unit, Small Animal Section, VRB.

Veterinary Resources Branch

Stephen Potkay, V.M.D.
Chief

The Veterinary Resources Branch provides professional and technical support service for NIH intramural programs. It is responsible for:

- Production of defined research animals
- Procurement, quarantine, conditioning, and issuance of animals from outside sources
- Management of central animal surgery and radiology facility
- Animal disease diagnosis and control
- Research holding for primates, cats, dogs, rodents and livestock
- Consultative services on animal health, care, husbandry, genetics, and nutrition
- Maintenance of an international laboratory animal Genetic Resource
- Administrative support of the Interagency Research Animal Committee and NIH Animal Research Committee.

While continuing to meet these responsibilities, the Branch increased its activities in evaluating its current programs and their overall usefulness to the NIH. An intensive effort was made, using contract services, to reassess current and projected NIH intramural program requirements for VRB services under the constraints imposed by employment limitations and by the application of full cost recovery accounting principles to service programs. Implementation plans were developed for those VRB activities where shifts in program emphasis were indicated. Another facet of the assessment was continuing evaluation of operating practices from the perspective of improving efficiency and productivity.

The Interagency Research Animal Committee (IRAC) and the NIH Animal Research Committee (NIHARC) continued to receive administrative support from VRB. At the request of the Office of Science and Technology Policy, IRAC drafted a document on animal care which was published as U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training. The Principles, endorsed by the nine U.S. Government agencies of IRAC, were incorporated into the revised PHS Policy on Humane Care and Use of Laboratory Animals by Awardee Institutions, and also appeared in the revised *Guide for the Care and Use of Laboratory Animals.* IRAC also drafted a National Chimpanzee Management Plan which was endorsed by NIH; it provides a means for establishing a self-propagating population of chimpanzees in this country to meet future research needs. IRAC continued to work with the Pan American Health Organization to assist Latin American countries to develop national primate plans designed to ensure preservation of wild populations and provide monkeys for biomedical research.

The NIHARC provided information and advice and served to coordinate activities of 14 BID Animal Research Committees. In cooperation with the NIH Training Center, NIHARC began a regularly scheduled course for intramural investigators on proper care and use of their animals. A more detailed discussion of the activities of the NIHARC follows in this DRS Annual Report.

Animal Center Section

The Animal Center Section purchases, maintains, and develops large laboratory animal models and provides related services and products for NIH investigators. The animals involved are mainly primates, farm animals, dogs, and cats. Monkeys, inbred miniature swine, and defined foxhounds, beagles, and pointers are provided by breeding colonies.

Long-term primate research holding continued as the Primate Unit's primary mission; project support was provided for the National Cancer Institute (NCI), the National Institute of Child Health and Human Development (NICHD), and the United States Army Medical Research Institute of Infectious Diseases. The latter involved a continuing interagency agreement with the Department of Defense, and a new agreement was developed with the Food and Drug Administration (FDA) to hold *Cebus* monkeys on a lipid-rich diet. The number of nonhuman primates acquired, quarantined, and released for investigative use remained relatively low. Total primate issues were about 700, with squirrel monkeys accounting for the majority.

The contract with the University of Miami to breed rhesus monkeys at Perrine, Florida, is being terminated because of reduced requirements for intramural projects of the NIH Bureaus, Institutes, and Divisions (BIDs). The colony will be sold intact, to permit it to continue serving as a resource for NIH's reduced level of needs and for those of other biomedical research programs.

There was a slight decrease in the number of ungulates used for antibody production, but the amount of normal blood issued increased significantly in support of artificial heart valve studies conducted by the National Heart, Lung, and Blood Institute (NHLBI).

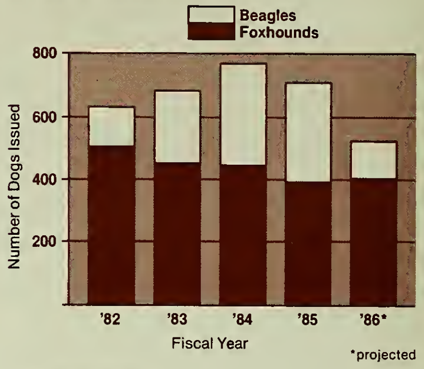
The NCI miniature swine herd continued to be maintained at approximately 250 head, although there were increases in both the numbers born and numbers used. Because of their unique genetic background, these inbred swine are valuable animal models for transplantation immunology and are in high demand by investigators at the NCI and elsewhere. Excess stock was provided to several institutes in the United States and one in France. A colony of 25 miniature swine used in atherosclerosis studies continued to be maintained for the NHLBI.

Canine programs, particularly breeding, underwent changes of the greatest magnitude at the Animal Center (Figure 1). Beagle breeding was discontinued halfway through the year at the request of the NCI, and the program will be entirely phased out early next year. Foxhound breeding was at the projected level, and more than 300 hounds were issued. The colony was reduced from 100 to 50 breeding bitches, and specifications were developed to allow the contract purchase of purpose-bred hounds to supplement production if necessary. Pointer colonies continued to be managed for the National Institute of Mental Health (NIMH); investigators reported good success in evaluating antianxiety agents using these dogs. Holding of beagles began for the National Eye Institute (NEI); they will be used for long-term studies of diabetic retinal degeneration. The principal health problem affecting the dog colonies was canine brucellosis. The epizootic was erradicated by testing and eliminating affected dogs.

A program evaluation of Carnivore Unit activities concluded that emphasizing dog research holding would provide greater benefit to the NIH than devoting the existing levels of space and other resources to breeding programs. Efforts were initiated to make the necessary program changes.

Numerous collaborative research projects were conducted. Those involving livestock dealt with artificial insemination, synchronization of estrus, and embryo transfer; they were undertaken to study and circumvent problems posed by cystic endometrial hyperplasia in swine, and to establish a flock of homozygous hyperbilirubinemic sheep. Participating institutions were the NCI, Clemson University, the Uniformed Services University of the Health Sciences (USUHS), the Smithsonian Institution (SI), and VRB. Efforts to improve reproduction among canids and felids were also continued in collaboration with USUHS and SI investigators; they involved the use of implanted GnRH-filled osmotic pumps to induce ovarian activity and estrus. Studies undertaken to determine optimal hormonal regimens for estrus induction and embryo transfer in cats resulted in the birth of two kittens, and *in vitro* fertilization studies were initiated using feline ova. A variety of projects were undertaken with investigators from NICHD, NIMH, and USUHS involving hormonal regulation of and the influence of light on reproduction in nonhuman primates, and studies on behavior and vocalization of newborn and adult New World monkeys were begun with NICHD. The Primate Unit also provided technical support to the NHLBI and the FDA for dietary studies of macaque and *Cebus* monkeys, respectively. Finally, work commenced to refine dietary formulations for callitrichids (marmosets and tamarins) to better meet their nutrient requirements.

Figure 1.
Issues of Research Dogs

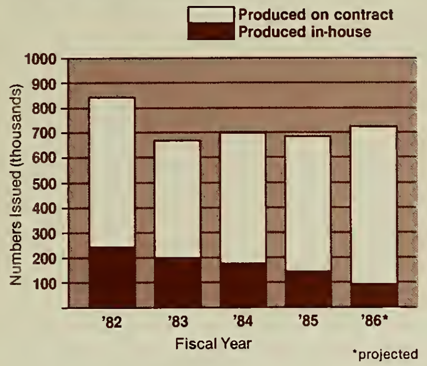


Small Animal Section

The Small Animal Section provides rodents and rabbits from its production colonies and also manages contracts for this purpose. It manages the NIH Animal Genetic Resource (NIHAGR), which contains more than 250 defined strains and stocks, and has programs devoted to animal model development, nutrition, health, embryo cyropreservation, and research holding.

Approximately 679,329 animals (144,417 from in-house and 534,912 from contractors) were issued, which is a 3 percent change from last year (Figure 2). The decline was related to

Figure 2.
Rodents and Rabbits Issued



several factors including a stabilization in small animal usage by BID investigators and a temporary decrease in availability of rats, guinea pigs, and hamsters related to unacceptable health quality.

No new supply contracts for rodents and rabbits were established, but a slight increase in the use of contractor-produced animals was noted. The delivery service contract for local pickup and delivery of small animals from regional airports was terminated during the year, because the number of animals shipped by air *vs* surface transportation from contract sources declined significantly.

The Animal Data Management System experienced several delays which resulted in postponing implementation of the program. The breeding, ordering, and inventory programs are expected to be available for testing early next year, however.

A series of management and program evaluation studies was conducted. Preliminary indications are that this process will culminate in recommendations for major program changes related to improving SAS products and services and the methods of delivering them as well as enhancing the cost effectiveness of various activities.

Changes in the composition of the NIHAGR varied by species. The breeding colony of *Mastomys* was lost through reproductive failure, and rabbit breeding stock carrying the Watanabe heritable hyperlipidemia (*whhl*) gene were established. A major effort was mounted to better define the Watanabe (*whhl*) colony in terms of its genetic and serum chemical characteristics, reproduction, and nutrition, as well as to develop techniques to improve its management and productivity. The cotton rat (*Sigmodon hispidus hispidus*) inbreeding program, begun several years ago, neared completion. Currently, 17th generation progeny are being produced. Development was completed on four congenic rats with the diabetes insipidus (*di*) gene—MNR/N-*di*, MR/N-*di*, OM/N-*di*, and ACI/N-*di*—and development of two Rowlett nude (*rnu*) congenic rats—SHR/N-*rnu* and RHA/N-*rnu*—reached the stage where issues became possible. The first LEW/N-*rnu* homozygous rats were issued during the year. The mouse program continued to be affected by the mouse hepatitis virus outbreak which occurred several years ago. The project to rederive mice in the barrier reached the 80 percent completion level, with all but one inbred, eight recombinant, and several congenic strains to be reestablished. Several of the rederived nude congenics reached the stage where issues were possible. Reflecting the increased interest by the research community in the beige mutation, this gene continued to be introduced into a number of inbred strains; the ultimate goal is to establish double (beige and nude) congenics. Likewise, investigators' interest in the X-linked immune defect (*xid* mutation was also high, and a project to form a double congenic involving the immunodeficient "motheaten" (*me*) and *xid* was undertaken. The request for new introductions into the NIHAGR continued, but only one mutant was successfully established because of isolator contamination in the gnotobiotic area. Requests for introduction of another 40 strains were delayed.

The animal health program focused on outbreaks of Sendai and rat coronavirus infections and neonatal deaths. The Sendai virus outbreak began in rats and necessitated cessation of breeding and issuing rats, hamsters, and guinea pigs for 16 weeks. Through relocating animals and intensive vaccination and testing procedures, the virus was finally eradicated. The rat coronavirus outbreak, confined to a limited area in the research holding facility, was eliminated by depopulation. A mortality rate of about 18 percent in the guinea pig colonies affected infants primarily; they succumbed to inanition, fetal atelectasis, and unexplained causes. Neonatal mortality in the rabbit colony reached 45 percent, and was characterized by similar findings.

The continued emphasis of the embryo cryopreservation program (ECP) was to enhance management of the NIHAGR. Program directives were twofold: cryobanking of murine embryos and continued developmental research to improve overall program efficiency through modification of current technology. More than 32,000 mouse embryos were collected, and over 7000 of them, from nine stocks and strains, were banked. They are intended for future implantation into foster mothers to avoid costly and time-consuming rederivation procedures and for studies of long-term survival. Developmental research provided data indicating that genotype has a strong influence on embryo output among stocks and strains subjected to a standardized gonadotropin regimen for ovulation induction, and that post-thaw survival of these embryos varied significantly among the stocks and strains evaluated. Another study demonstrated that a commonly used gas sterilant, ethylene oxide, is toxic to embryos during *in vitro* culture if containers are not adequately aerated following its use. A collaborative effort was also initiated with NICHD to utilize the resources of the ECP in transgenic mouse embryo cyropreservation and research.

The scope of nutrition-related activities was broadened to include large research animals as well as small. Ongoing studies involving nonhuman primates resulted in developing open formula diets suitable for macaques and callitrichids, and planning is under way to work with dogs in the coming year. Major new projects were initiated in collaboration with investigators from the NHLBI and NEI, and assistance continued to be provided at NIH and elsewhere in designing and conducting experiments with nutritional components. The branch nutritionist was also active on NIH's Subcommittee on Nutrition Education, which reviews all NIH publications containing nutrition information intended for public distribution.

The number of animal research holding days increased by 10 percent, and 61 investigators from 12 BIDs utilized the facility. SAS employees performed most of the technical procedures for these investigators. Full occupancy was not achieved due primarily to the detection of rat corona and Sendai virus titers. The gnotobiotics staff performed 304 hysterectomies for introductions into the barrier and germfree isolators. Approximately 225 germfree rats and mice were distributed to NIH contractors as replacement breeder stock, and new rat and mouse strains were received for introduction into the genetic resource.

Comparative Pathology Section

The Comparative Pathology Section characterizes the health status and studies the naturally occurring diseases of laboratory animals produced, quarantined, or utilized at the NIH. Through its Animal Disease Investigation (ADI) service, it provides diagnostic services as well as consultation and advice on animal colony management. It also manages a program to ensure the genetic quality of animals provided by NIH for use as breeders to other institutions throughout the world.

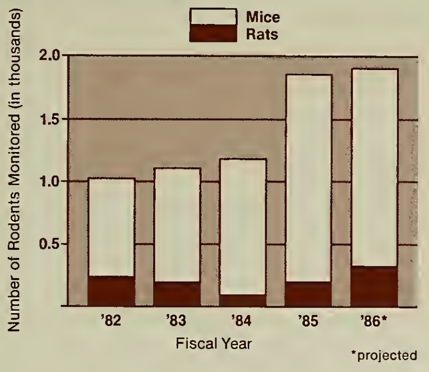
The number of necropsies performed by the pathology service was 21 percent less than last year, due largely to the absence of the major disease outbreaks. As in past years, a large number of guinea pigs and rabbits were stillborn, and although cecitis in rabbits remained a significant problem, there were no massive outbreaks. Many necropsies were performed for NIH investigators through the ADI service, and assistance was provided to investigators in distinguishing naturally occurring diseases from experimentally induced conditions.

The number of samples processed by the microbiology service dealing with bacteriological culturing and in-house serology was 74 percent higher than last year. The increase was related to the counting of in-house serology samples for the first full year. Enzyme-linked immunosorbent assays (ELISAs) for *Bacillus piliformis* and cilia-associated respiratory (CAR) bacillus were added to the routine battery of in-house serologic tests. Application of these tests indicated that the production and genetic resource colonies of mice and rats were free of CAR bacillus, but evidence of infections was found in the rabbit colonies. Rats with serum antibody to *B. piliformis* were found in one room, but no clinical signs or gross lesions suggestive of Tyzzer's disease were observed. Studies are under way to investigate the cause of the titers, but similar findings of *B. piliformis* antibody in rats by researchers in Japan and Europe usually have remained unexplained despite extensive investigations. The number of samples received by the clinical pathology service for endo- and ectoparasite monitoring, hematology, and contracted virus monitoring was virtually unchanged compared to previous years.

The ADI service responded to 343 calls for assistance from the BIDs. This was approximately 23 percent lower than last year, and the decrease is believed to be related to the assumption of considerable clinical work by veterinarians newly assigned to several of the Institutes.

The number of permits for introductions of rodents and rodent products from sources other than those approved by the Small Animal Section was 46 percent higher than last year. Since the number of permits varies with the activities of the BIDs, it tends to change from year to year. Of the permits issued, 13 required

Figure 3.
Genetic Monitoring



*projected

that rodents be quarantined in SAS facilities at Poolesville, 27 required quarantine by the BIDs, and 11 did not require quarantine.

Approximately 200 rats and 1650 mice from the foundation, pedigreed expansion, and production colonies were monitored for genetic integrity. No genetic contaminations were reported or detected in any of the genetic resource colonies. The 58 percent increase over the total number of animals monitored last year was the largest annual increase since the program was established (Figure 3). It was attributable to expansion in the number of mouse strains routinely monitored by the laboratory, including congenic strains in the Genetic Resource, and F1 hybrids animals from the production colonies. Starch gel electrophoresis is being replaced with cellulose acetate electrophoresis as the basic methodology in the laboratory. This, coupled with modifications in administrative procedures, should improve efficiency by decreasing requirements in the areas of tissue storage, scheduling, and record keeping, and allow the Unit to better cope with its workload. It is anticipated that the total number of requests for assistance under the Genetic Investigation Service will remain constant at approximately 25 per year.

Research activities were concerned with studies of the pathogenesis of diseases occurring in the animal colonies, their control, and the development of methods for monitoring infectious agents and genetic purity. Specific studies were directed towards determining the pathogenesis of cilia-associated respiratory (CAR) bacillus infections, developing genetic profiles for inbred laboratory rodents, developing mouse and rat isozyme systems using isoelectric focusing with polyacrylamide and agarose gels, and, in collaboration with the FDA, developing a standard strain of mice for pertussis vaccine bioassays.

Although no major changes are anticipated, it is recognized that some adjustments in the current programs will be needed to accommodate changes in the kinds and levels of support required for BID programs and VRB in-house activities.

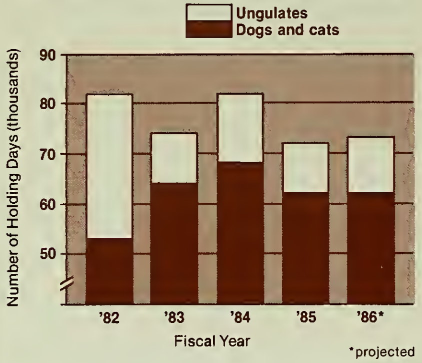
Veterinary Medicine and Surgery Section

The Veterinary Medicine and Surgery Section provides centralized facilities for experimental surgery and research animal holding. It makes available routine care and comprehensive veterinary support for animals housed in the Section, and provides consultative services to intramural investigators regarding development and use of animal models.

The Surgery Unit supported approximately 1000 cases, as it did last year. Major efforts were applied toward the development of animal models of *spina bifida* and neovascularization of the myocardium. *Spina bifida* can result in severe neural defects, and fetal rhesus monkeys were used *in utero* for studying its pathogenesis and treatment. A modified Vineberg technique was used in dogs to transplant the internal thoracic artery into the myocardium, so that angiogenesis factor could be infused continuously through an implanted pump. The potential for subsequent neovascularization of the myocardium is being evaluated by the NHLBI as a possible treatment for myocardial infarcts. Other major projects included studies of the survival time of fetal grafts in allogenic hosts and thymic regulation of fetal ovarian/adrenal differentiation in primates.

The majority of the dogs, sheep, and swine held by the Comparative Medicine Unit were used as models in research related to cardiovascular diseases and cancer therapy, while cats were used in increasing numbers by the National Institute of Neurological and Communicative Disorders and Stroke as models for vascular stroke and for surgical or chemical alterations of the nervous system (Figure 4). Studies of Parkinson's disease in beagles and of avian malaria in chickens were continued by the NIMH and National Institute of Allergy and Infectious Diseases, respectively, and a long-term project was begun which utilizes foxhounds to investigate the extent of alveolar deterioration secondary to periodontal disease. Nonhuman primates continued to be available through the recycle program, but the utilization rate was extremely low.

Figure 4.
Large Research Animal Holding—Bethesda



Demand for holding space in the Primate Research Unit declined slightly, the average number of animals held being about 900. Primate holding next year is expected to remain about the same, but space requirements are expected to change as a result of the need to house large baboons for the NHLBI, provide isolator units for special NINCDS studies, and install large caging in which animals can be observed by behavioral changes resulting from surgically created neurologic deficits. At the same time, there appeared to be a trend towards using more sophisticated support equipment such as flexible metal tethers to protect implanted catheters in unrestrained animals, and reservoir assemblies to deliver medication by way of the automatic watering systems.

Forecast

Prices for many animals and related products will increase significantly as a result of implementing an NIH-wide full cost recovery accounting system. An overall decline in the utilization of research animals, particularly those produced by VRB, is projected. Emphasis will be placed on redirecting various activities from production to research holding both to meet expressed BID requirements and to improve the cost effectiveness of VRB programs. Concurrently with these anticipated changes, a major renovation project will be undertaken to improve housing for the NIHAGR, permit consolidation of small animal production activities, and expand capabilities for research holding. A facility for housing miniature swine is also planned. It is expected that the Branch will contribute further, through the NIH Animal Research Committee, to identifying and proposing solutions to issues concerning animal care and use at the NIH.

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Udelsman, R., Bacher, J.D., Gallucci, W.T., Gold, P.W., Morin, L.R., Renquist, D.M., Loriaux, D.L., Chrousos, G.P.: Hemodynamic and endocrine parameters in the anesthetized cynomolgus monkey: A primate model. *J. Med. Primatol.,* 13:327-338, 1984.

Waggie, K.S.: Diagnosis of Tyzzer’s disease in a laboratory animal colony. *Synapse* 18:12-13, 1985.

The NIH Animal Research Committee

Thomas L. Wolfle, D.V.M., Ph.D.
Executive Secretary

Animals used in biomedical and behavioral research have received considerable attention during recent years both in the scientific community and in public forums at home and abroad. The issue has often been a volatile one, and the atmosphere highly charged, because of the great diversity of opinions on all aspects of animal care and use. The situation can perhaps be more readily appreciated though a few examples illustrative of recent activities undertaken on the domestic and international scenes that reflect current desires of the public and scientists as reflected by the actions of governmental bodies.

U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training, which were developed by the Interagency Research Animal Committee, were recently promulgated by the U.S. Office of Science and Technology Policy, and a similar document was presented for adoption to the World Health Organization by the Council for International Organization of Medical Sciences. National legislation on this subject is currently being revised by many European countries, and, after several years of development, a Convention for the Protection of Vertebrate Animals Used for Experimental Purposes is expected to be ratified soon by member nations of the Council of Europe. Lastly, long-standing Department of Health and Human Services policies, guidelines, and principles, as expressed in the "Public Health Policy on Humane Care and Use of Laboratory Animals by Awardee Institutions" and the *Guide for the Care and Use of Laboratory Animals,* have been revised and will be implemented early in fiscal year 1986.

The NIH Animal Research Committee (NIHARC) provides the NIH scientific community with a focal point for discussing issues of animal care and use, assisting in the implementation of Departmental policy, and serving as a review body for drafting or commenting on proposed policies. It consists of the chairpersons and their alternates from the Animal Research Committees of NIH Bureaus, Institutes, and Divisions (BIDs). The Acting Director, DRS, serves as the Chairman of the NIHARC as well as the Interagency Research Animal Committee. Administrative and support staff for both committees are provided by the Veterinary Resources Branch, DRS.

The NIHARC has been instrumental in effecting major changes in animal care within NIH intramural programs. It has provided cohesiveness to individual BID ARCs, enabling the NIHARC to undertake initiatives which the BID ARCs should not accomplish alone. Although members of a farsighted Scientific Director's meeting in 1971 approved the creation of ARCs (then called Animal Care Committees) and, in 1977, established a goal of accreditation for each BID's animal facilities, no charter or specific mandates were issued. For the most part, these goals remained elusive until the NIH Manual Chapter 3040-2, *Animal Care and Use in the Intramural Program,* was adopted and implemented in December 1983. BID ARCs include scientists, a veterinarian, and a nonscientist from outside the institute. The committees' express purpose is to keep Scientific Directors informed of animal care and use practices within their BIDs and to ensure that NIH intramural programs meet the same high standards of animal care and use NIH requires from extramural grantees and contractors. To this end, the committees meet to review research proposals, site visit the animal facilities, discuss management options and issues of humane care and use, and, in general, provide troubleshooting assistance and advice both to investigators and to the Scientific Directors. The most significant step in this process is the annual report, submitted to the Deputy Director for Intramural Research, which summarizes activities of the committees in general and addresses any facility and management deficiencies that hinder the BID's ability to seek accreditation by the American Association for Accreditation of Laboratory Animal Care. These reports provide on accurate reflection of the strengths and weaknesses of animal care and use within the intramural program. As a direct result of these reports the Director, NIH, established task forces within each BID and a target date of October 1987 to bring intramural facilities into complete compliance with the *Guide* so as to enable AAALAC accreditation soon thereafter.

Since the NIHARC represents a knowledgeable resource on animal care and use to NIH management, the committee is often called upon to provide advice or information, to review draft policy proposals, and to implement policy.

The following examples provide an indication of the type and breadth of these activities:

- NIH policy stipulates the NIHARC's responsibility for developing and coordinating training programs for NIH employees on animal care and use. To implement this objective, an NIHARC subcommittee on training was established, lesson plans and speakers selected, and presentations critiqued before delivery to the first class. The National Capital Area Branch of the American Association for Laboratory Animal Science provided valuable assistance in this process. Half-day courses are now presented quarterly, in cooperation with the NIH Training Center, to new investigators and animal technicians. They are designed to assist these researchers in the humane handling and care of the animals they use, while increasing their awareness of social issues and obligations related to humane care and use.
- Because of the structure of the NIH, it is difficult to develop accurate information of the numbers, species used, locations, and space required for animals used in intramural programs. The NIHARC completed surveys this year tabulating such information, which has been of value in a number of situations. Both on-campus and off-campus populations of NIH-owned animals in support of intramural programs were identified and enumerated for review by the Scientific Directors, the Office of Space Management, and the NIH architect. The NIH Master Plan requires periodic review of all space, of which animal and support rooms are important considerations. Because a number of institutes maintain animals in the Clinical Center, these surveys have assisted its Director and other BID Scientific Directors to begin looking at ways to centralize the management of these areas, an issue of critical importance to accreditation of any BID with animals in this building.
- Pest control and laundry procedures, often viewed as routine, are actually essential components in providing good animal care. They were reviewed and discussed, and perspectives of the NIHARC assisted in refocusing and enhancing the effectiveness of these activities.
- A subcommittee of the NIHARC, consisting of veterinarians with responsibility for animals maintained in the Clinical Center, was appointed to consider the special features of animal holding, management, and facilities in this large, multi-use building. This subcommittee is actively addressing some of the many long-standing animal-related challenges posed by this facility.
- An essential activity of the NIHARC is to coordinate the annual NIH composite report to the United States Department of Agriculture (USDA), as required under the Animal Welfare Act. Because the USDA issues no directions or guidance for completing this form, the Committee developed NIH guidelines, which address such difficult issues and definitions as "pain," "distress," and "use" and procedures that should be considered painful or stressful. Even though these working guidelines continue to evolve, their value was recognized this year by the USDA, which sent them nationwide to reporting facilities as suggested guidelines.

The NIHARC and the Office of the Executive Director, IRAC, have played an important role in improving NIH practices involving research animal care and use through providing coordination, information, and advice to each of the 14 BID committees. This next year should see continued growth and involvement of these NIH intramural committees in establishing and guiding animal related policies that are consistent with the needs of science and responsive to public concern. It is anticipated that the NIHARC will continue to contribute to defining state-of-the-art in the practice of animal care and use, helping the NIH achieve them, and providing leadership in this field to the scientific community at large.

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VETERINARY RESOURCES BRANCH
DIVISION OF RESEARCH SERVICES
NATIONAL INSTITUTES OF HEALTH (U.S.)

FY 1985 VRB ANNUAL REPORT

Dr. Stephen Potkay, Chief

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VRB Research Projects (Z01 RS)

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DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00051-06 VR

PERIOD COVERED

October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Reproduction in Mutant Sheep Used for the Study of Hyperbilirubinemia

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	L.D. Stuart	Chief	UU, ACS, VRB, DRS
Others:	D.E. Wildt	Guest Worker	VRB, DRS
	S.C. Kalser	Director	Liver Diseases Prog., DDN, NIAID
	P.K. Chakraborty	Head	Res. Division, Dept. of OB-GYN, USUHS

COOPERATING UNITS *(if any)*

Digestive Diseases and Nutrition Program, National Institutes of Arthritis, Metabolism and Digestive Diseases.

LAB/BRANCH

Veterinary Resources Branch

SECTION

Animal Center Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.2	.1	.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A specific genetic strain of Corriedale sheep is used as an animal model for the study of liver pathophysiology, specifically, hyperbilirubinemia (Dubin-Johnson Syndrome). This project is concerned with increasing the numbers of animals available for research by the controlled breeding of individuals which genetically transmit this character. This project is utilizing what is considered to be the only existing Corriedale sheep homozygotic for this trait. Efforts are being made to obtain both homozygous and heterozygous offspring from these highly inbred individuals. Semen collected artifically from rams is diluted in various cryoprotective extenders and then freeze preserved. This will ensure the long-term availability of male gametes for artificial insemination. Overall, this project allows perpetuation of this specific gene pool and ensures availability of research animals for future investigations of Dubin-Johnson Syndrome and related metabolic disorders.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 00067-03 VR

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Hematologic and Serum Chemical Characteristics of Aotus sps.

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	D.M. Renquist	Chief	PU, ACS, VRB, DRS
Others:	R.W. Atwell	Bio. Lab. Tech.	PU, ACS, VRB, DRS

COOPERATING UNITS *(if any)*
None

LAB/BRANCH
Veterinary Resources Branch

SECTION
Animal Center Section

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER
.2	.2	0

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Hematologic and serum chemical characteristics of 120 Aotus monkeys were determined to acquire information which may be useful in the care of these animals. This information may also be useful in determining the usefulness of this species as an animal model. The monkeys were bled every four months for one year. The hematologic and serum chemical characteristics are being statistically analyzed.

This project was discontinued January 1, 1985.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00069-03 VR

PERIOD COVERED

October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Anthropometric Study of the Aotus grisemembra and Aotus trivirgatus

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	D.M. Renquist	Chief	PU, ACS, VRB, DRS
Others:	D. Barnard	Nutritionist's Assist.	SAS, VRB, DRS

COOPERATING UNITS *(if any)*

None

LAB/BRANCH

Veterinary Resources Branch

SECTION

Animal Center Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER
.10	.10	0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this study is to establish anthropometric parameters for assessing normal growth of Aotus monkeys in captivity, to assess alteration in the development of experimentally treated animals, and to provide an age estimation for primates with unknown birth dates. The anthropometric and dental data collections were made on a regular basis until the animals reached maturity. The anthropometric measurements entailed head length, head breadth, crown-rump length, foot length, hand length, bitrochanteric diameter and overall length. It has been determined that weights at six months were between 402 and 563 grams, approximately half that of the adults. Deciduous tooth eruption patterns are similar to other nonhuman primates. It has been observed that the growth rate plateaus at one year and six months of age. The anthropometric measurement correlating most closely with increasing age is the bitrochanteric diameter.

This project was completed January 1, 1985.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00070-01 VR

PERIOD COVERED

October 1985 to March 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Effect of Tocainide HCl Pretreatment of Surface-Induced Cardiac Hypothermia

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	M. April	Chief	CU, ACS, VRB, DRS
Others:	J.C. Keith	Assist. Professor	VMRCVM (VA-MD Regional College Vet. Med.)
	P. Ruggera	Products Engineer	FDA, Center for Devices & Rad. Health
	J. Gainer	Assist. Br. Chief	FDA, Center for Veterinary Medicine
	K. Roberts	Assist. Professor	VMRCVM (VA-MD Regional College Vet. Med.)
	G. Kantor	Chief Physicist	FDA, Center for Devices & Rad. Health

COOPERATING UNITS *(if any)*

Food and Drug Administration, Centers for Veterinary Medicine, and Devices and Radiological Health
VA-MD Regional College of Veterinary Medicine

LAB/BRANCH

Veterinary Resources Branch

SECTION

Animal Center Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER
0.025	0.025	0.012

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
 ☐ (a1) Minors
 ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Studies with the beagle dog as the animal model will be conducted to ascertain the myocardial cytoprotective effects and antiarrhythemic effects of the new drug tocainide HCl (which is an orally active form of lidocaine HCl); and the rapid rewarming effects produced by a radio-frequency (RF) helical coil. Hypothermic studies (using beagle dogs) were also initiated to evaluate the effectiveness and safety of the RF coils to simulate rewarming human hypothermia casualties.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 00071-01 VR

PERIOD COVERED

October 1, 1984 to September 30, 1985

TITLE OF PROJECT (80 characters or less)

Development of Genetic Profiles for Inbred Laboratory Rodents

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

J.S. Crowell, Geneticist	Comparative Pathology Section, VRB, DRS
K.P. Smith, Geneticist	Comparative Pathology Section, VRB, DRS
S.L. Finley, Biochemist	Comparative Pathology Section, VRB, DRS

COOPERATING UNITS (if any)

Small Animal Section, VRB, DRS

LAB/BRANCH

Veterinary Resources Branch

SECTION

Comparative Pathology Section

INSTITUTE AND LOCATION

Division of Research Services, Bethesda, Maryland 20892

TOTAL MANYEARS: 0.5	PROFESSIONAL: 0.4	OTHER: 0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

This project is designed to identify and locate on the chromosomes of inbred rodents inherited characteristics which can be used in a wide range of biomedical research and to further the ability of the Genetic Monitoring Unit to perform its basic mission. The major areas of interest are: 1) characterization of the genetic traits by biochemical and immunological techniques; 2) chromosome mapping by standard genetic analysis; and 3) application of the genetic characteristics to explore new animal models of pathogenesis.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00072-01 VR

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Pathogenesis of cilia-associated respiratory (CAR) bacillus infections

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

K. S. Waggie, D.V.M., Ph.D.	Comparative Pathology Section, VRB, DRS
A. M. Allen, D.V.M., Ph.D.	Comparative Pathology Section, VRB, DRS
A. Lock, D.V.M., M.S.	Comparative Pathology Section, VRB, DRS
T. H. Spencer, B.S.	Comparative Pathology Section, VRB, DRS

COOPERATING UNITS *(if any)*
None

LAB/BRANCH
Veterinary Resources Branch

SECTION
Comparative Pathology Section

INSTITUTE AND LOCATION
Division of Research Services, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER.
0.4	0.1	0.3

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The cilia-associated respiratory bacillus was first demonstrated with silver stains of sections of the respiratory tract of rats by workers in the Netherlands. It was isolated in embryonated hen's eggs by staff of Comparative Pathology Section (Inf. and Immun., Feb. 1985) as a result of efforts to diagnose and characterize chronic respiratory disease in rats from an investigator's lab at NIH. To date the agent has not been grown on cell-free media. Because of its gliding, flexing motion in the absence of evidence of means of locomotion, it is believed to be a member of the group of gliding bacteria. Preliminary pathology studies indicate that infections in rats result in chronic respiratory disease.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 00073-01 VR

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Lipid Metabolism of the Macaca Fascicularis

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	D. Barnard	Biologist	SAS, VRB, DRS
Others:	J. J. Knapka	Nutritionist	SAS, VRB, DRS

COOPERATING UNITS *(if any)*
VMSS

LAB/BRANCH
Veterinary Resources Branch

SECTION
Small Animal Section

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.5	.5	1

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The study will examine the metabolism of exogenous fatty acids by Macaca fascicularis. Trans fatty acids which can not be synthesized by eukaryotes will be used as the exogenous fatty acid marker. Trans fatty acids are geometrical isomers of cis-fatty acids which can be synthesized by eukaryotes. Trans fatty acids are not toxic as long as the essential fatty acid requirements are satisfied. The trans fatty acids are catabolize and removed from the body shortly after they are removed from the diet.

Twelve male Macaca fascicularis monkeys will be used in the study. Six of the monkeys will be fed the control diet and the others will be fed the experimental diet containing trans fatty acids. Thirty-six weeks will be required to complete the study.

The objectives of the study are to:

1) Determine if the monkeys have the gut flora required to produce trans fatty acids.

2) Determine if trans fatty acids are incorporated into the RBC membrane of the monkeys.

3) Determine if the trans fatty acids incorporated into the RBC membrane effect the membrane function by examining a membrane-bound enzyme.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 00074-01 VR

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Lipid Metabolism of the Macaca Fascicularis

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	J. J. Knapka	Nutritionist	SAS, VRB, DRS
Others:	D. Barnard	Biologistist	SAS, VRB, DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH
Veterinary Medicine and Surgery Section

SECTION
Small Animal Section

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS: 1.25	PROFESSIONAL: 0.25	OTHER: 1.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A continuing program in laboratory animal nutrition involves studies with the species that are most frequently used as animal models in biomedical research. The objective of the program is to improve the nutritional status of NIH production and research colonies of rats, mice, guinea pigs, rabbits, dogs, cats and various species of nonhuman primates. A series of functional designed feeding trials are used to ascertain the nutrient requirements of the species of interest and to develop diets with more nearly optimal nutrient concentrations for their growth, reproduction, maintenance or general health status. This program has resulted in the development of open formula natural ingredient diets for all animal species maintained in significant numbers at NIH except dogs and cats.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00075-01 VR

PERIOD COVERED

October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Effect of Diet on Cataract Incidence in Rats with Hereditary Retinal Dystrophy

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	J. J. Knapka	Nutritionist	SAS, VRB, DRS

COOPERATING UNITS *(if any)*

Retinal and Ocular Connective Tissue Diseases Section Chemical Branch, NEI

LAB/BRANCH

Veterinary Resources Branch

SECTION

Small Animal Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.6	.1	.5

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A series of feeding trials were conducted where different types of diets or diets formulated with graded levels of single nutrients or varying concentrations of specific ingredients were fed to RCS rats. The criterion of evaluation was the development of cataracts in the test animals. Results of these trials indicated cataract incidence is influenced by dietary constituents, at least in the rat. The use of fishmeal in the formulations of either purified or natural ingredient diets markedly increased cataract maturity. Increased dietary calcium concentrations also increased cataract incidence but to a lesser extent than the fishmeal.

Discontinued.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 00076-01 VR

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Zinc Deficiency in S. mystax and its relationship to Wasting Marmoset Syndrome

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	D. E. Barnard	Biologist	SAS, VRB, DRS
Others	D. M. Renquist	Unit Chief	PU, ACS, VRB, DRS
	J. J. Knapka	Nutritionist	SAS, VRB, DRS

COOPERATING UNITS *(if any)*
Small Animal Section

LAB/BRANCH
Veterinary Resources Branch

SECTION
Animal Center Section

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.40	.30	.10

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this study was to determine if the etiology of Wasting Marmoset Syndrome (WMS) is related to zinc deficiency. The clinical symptoms of zinc deficiency and WMS are very similar. It was determined that S. mystax exhibiting signs of WMS were zinc deficient. The study involved feeding two diets to several wasting S. mystax, one diet was supplemented with zinc carbonate and the other was not. Serum zinc concentrations and blood chemistries were sampled on a regular basis. Tissue were taken from dead tamarins for zinc analysis.

The S. mystax is an invaluable laboratory animal model for immunological research. However, in captivity, many of these tamarins are unable to breed and eventually die due to WMS. The fact that S. mystax are zinc deficient may provide an answer to the etiology of WMS.

This project has been discontinued. It was found dietary zinc had no effect on WMS and the data have been incorporated into another paper.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

Z01 RS 00077-01 VR

PERIOD COVERED
October 1, 1984 to September 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Development of an Embryo Cryopreservation Program in Laboratory Animals

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	Patricia M. Schmidt	Research Physiologist	SAS, VRB, DRS
Others:	David E. Wildt	Guest Researcher	VRB, DRS
	Carl T. Hansen	Geneticist	SAS, VRB, DRS
	Mitchel C. Schiewe	Guest researcher	VRB, DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH
Veterinary Resources Branch

SECTION
Small Animal Section

INSTITUTE AND LOCATION
DRS, NID, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
3.5	2.5	1

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The objective of this program is to facilitate the management of the NIH Animal Genetic Resource (NIHAGR) through development and utilization of embryo collection, culture, freezing and transplantation as techniques for cryobanking genetic stock and improving reproductive potential. Embryos are frozen slowly in medium containing cryoprotectant to allow sufficient dehydration of embryos to insure post-thaw survival. Following dilution of cryoprotectant after thawing, embryos are cultured to assess in vitro development. Embryos are collected and maintained in a frozen state until needed for rederivation of stocks and strains. This reduces genetic drift and serves to safeguard live colonies from catastrophe. Development of this technology allows banking of embryos for long-term storage and subsequent rederivation under the direction of the Geneticist, SAS. Concurrent comparative research studies are designed to identify modifications in methodology which will enhance female response to ovulation induction regimens and improve post-thaw embryo viability.

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